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(71) Applicant (for AE, AG, AU, BB, BZ, CA, CY, GB, GD, GH, GM, IE, IL, KE, LC, LK, LS, MN, MW, NZ, SD, SG, SL, SZ, TT, TZ, UG, ZA, ZW only): **UNILEVER PLC** [GB/GB]; Unilever House, Blackfriars, London EC4P 4BQ (GB).

(71) Applicant (for AL, AM, AT, AZ, BA, BE, BF, BG, BJ, BR, BY, CF, CG, CH, CI, CM, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, FR, GA, GE, GN, GQ, GR, GW, HR, HU, ID, IS, IT, JP, KG, KP, KR, KZ, LR, LT, LU, LV, MA, MC, MD, MG, MK, ML, MR, MX, MZ, NE, NL, NO, PL, PT, RO, RU, SE, SI, SK, SN, TD, TG, TJ, TM, TR, UA, UZ, VN, YU only): **UNILEVER NV** [NL/NL]; Weena 455, NL-3013 AL Rotterdam (NL).

(71) Applicant (for IN only): **HINDUSTAN LEVER LIMITED** [IN/IN]; Hindustan Lever House, 165/166 Backbay Reclamation, Mumbai 400 020, Maharashtra (IN).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **CARINA, Riccardo, Filippo** [IT/CH]; 1, rue Joseph Pasquier, CH-1203

Geneve (CH). **GIBSON, Carl** [GB/GB]; Unilever Research Port Sunlight, Quarry Road East, Bebington, Wirral, Merseyside CH63 3JW (GB). **WHITTAKER, Jane** [GB/GB]; Unilever Research Port Sunlight, Quarry Road East, Bebington, Wirral, Merseyside CH63 3JW (GB).

(74) Agents: **ELLIOTT, Peter, William** et al.; Unilever PLC, Patent Department, Colworth House, Sharnbrook, Bedford, Bedfordshire MK44 1LQ (GB).

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(54) Title: MACROCYCLIC TETRAAMIDO LIGANDS AS BLEACHING CATALYSTS AND SYNTHESIS THEREOF

(57) Abstract: The invention relates to a novel synthetic route for a group of ligands and to an improved catalyst containing the ligand. It provides a method for the synthesis of a ligand having the structure: (I) The invention also provides use of a ligand for inhibiting dye transfer.



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MACROCYCLIC TETRAAMIDO LIGANDS AS BLEACHING CATALYSTS AND SYNTHESIS THEREOF

**Field of the Invention**

5 The present invention relates to the synthesis and use of macrocyclic metal-ligand complexes as bleaching catalysts. In particular it relates to a novel synthetic route for a group of these ligands and to an improved catalyst  
10 containing the ligand.

**Background of the Invention**

15 Oxidation catalysts comprising metal-complexes are well known. One class being macrocyclic ligands, which co-ordinate with a transition metal ion. Such catalysts have been used in laundry compositions as parts of a bleaching system. These catalysts activate  $H_2O_2$  or other peroxygen  
20 sources in water, and are effective at neutral to basic pH.

A catalyst is disclosed in WO 98/03263, filed 21 July 1997, (Collins), which comprises a macrocyclic (tetra) amido N-donor. The macrocycle is capable of complexing with a metal  
25 ion, for example an iron III or IV. The complex also comprises axial ligands, for example as chloride or water, and one or more counter ions, for example tetraphenylphosphonium and tetraethylammonium.

30 United States Patent 5,853,428, filed 24 Feb 1997, (Collins) discloses use of similar catalysts in laundry detergent compositions.

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Bleaching catalysts are of particular utility in the prevention of so-called 'dye transfer'. This occurs when dyestuffs are released from one region of a cloth article during laundering and later re-adsorbed at another location or on another article. It is advantageous to bleach the  
5 dyestuff while it is in aqueous solution, thereby preventing or reducing its transfer.

For reasons of toxicological and environmental acceptance,  
10 it is preferable that the axial ligands and counter-ions are relatively benign. Ions such as trifluoroacetate, tetraphenylphosphonium and tetra-ethylammonium are not preferred where they would typically come into skin-contact as a consequence of use.

15 Several synthetic routes are known for the preparation of the catalysts described in the 'Collins' patents. In one such route, described in United States Patent 6,051,704, Filed 22 July 1996, an alpha or beta amino carboxylic acid,  
20 for example a alpha-amino isobutyric acid, is reacted with an activated malonate or oxalate derivative, for example a di-methyl malonyl chloride, with mild heating. Upon completion of a double coupling reaction, hydrolysis of the product yields a diamine-containing intermediate, a macro  
25 linker. In a further step, a diamine, typically an ortho-phenylene diamine, is reacted with the macro linker in the presence of a coupling agent to form a tetra-amido macrocycle. The macrocycle is subsequently complexed with a metal in the presence of appropriate ligands.

30 The synthetic route described in the 'Collins' patents is believed to produce a relatively low yield of a relatively

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impure material, and is believed unsuitable for large scale use.

An azide based synthetic route to macrocyclic tetra-amido  
5 ligands is described in Uffelman, E. S., PhD Thesis  
(California Institute of Technology, [1992]). This is  
described in further detail in United States Patent  
5,853,428, filed 24 Feb 1997.

10 A further synthetic route is disclosed in US 6127536 (Deline  
et al., filed May 25<sup>th</sup> 1999, issued October 3<sup>rd</sup> 2000). In  
this synthesis 1,2-phenylenediamine is reacted with 2-  
bromoisobutyryl bromide to form a precipitating intermediate  
which is cyclised by reaction with diethyl malonyl  
15 dichloride.

#### Summary of the Invention

20 We have determined how an alternative synthetic route can be  
applied to obtain an improved yield of a ligand, which is  
believed to contain low levels of impurities. Furthermore,  
this yield and purity enables the formation of complexes in  
which the axial ligand is chlorine or water.

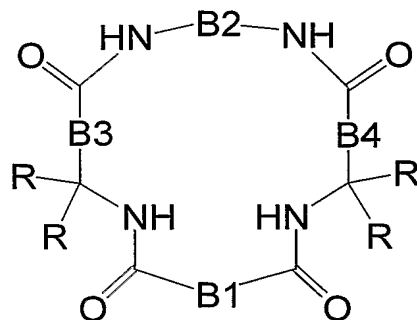
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In simple terms, this route employs an N-protected amino  
acid, which is first reacted, at its carbonyl end, in the  
form of an acid chloride, with a diamine and subsequently  
deprotected to produce a macro-linker with available amino  
30 groups. This macro-linker is reacted with a di-carbonyl  
species to form the macrocycle. This differs from the prior  
route in which the macro-linker is formed by reaction at the

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amino group of the acid and subsequent ring closure occurs across the carbonyl groups of the amino acid residue.

Accordingly, a first aspect of the present invention provides a method for the synthesis of a ligand having the structure:



wherein:

- B<sub>1</sub>, B<sub>3</sub> and B<sub>4</sub> each represent a bridging group having zero, one two or three carbon containing nodes for substitution, and B<sub>2</sub> represents a bridging group having at least one carbon containing node for substitution, each said node containing a C(R), C(R<sub>1</sub>)(R<sub>2</sub>) or C(R)<sub>2</sub>,
- each R substituent is the same is the same or different from the remaining R substituents and
  - (i) is selected from the group consisting of alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, alkynyl,

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alkylaryl, halogen, alkoxy, phenoxy and combinations thereof, or

- 5 (ii) form a substituted or unsubstituted benzene ring of which two carbons on the ring form nodes in the B-unit,

said method comprising the steps listed below in the order given

10

a) protecting the amino group of an amino acid comprising  $\text{HOOC-B}_3\text{-CRR-NH}_2$  and/or  $\text{HOOC-B}_4\text{-CRR-NH}_2$ ,

15

b) activating the carbonyl group of said amino acid,

c) reacting the carbonyl-activated amino acid with a diamine  $\text{H}_2\text{N-B}_2\text{-NH}_2$  to form a diamide diamine,

20

d) deprotecting said protected amino groups, and,

e) reacting the de-protected diamide diamine with an activated di-carbonyl compound to form a tetra-amine macrocycle.

25 It is preferred that  $\text{HOOC-B}_3\text{-CRR-NH}_2$  and  $\text{HOOC-B}_4\text{-CRR-NH}_2$  in step a) are the same.

30

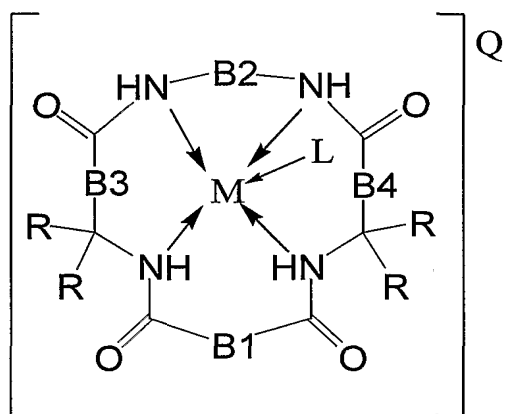
The aforementioned synthetic method is not restricted to  $\text{B}_1$ ,  $\text{B}_2$ ,  $\text{B}_3$  and  $\text{B}_4$  as defined above. One skilled in the art will appreciate the  $\text{B}_1$ ,  $\text{B}_2$ ,  $\text{B}_3$  and  $\text{B}_4$  may represent any suitable spacing group that does not prevent the synthetic method from proceeding. Where required a group that does inhibit the reaction is protected. The particular length  $\text{B}_1$ ,  $\text{B}_2$ ,  $\text{B}_3$

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and B<sub>4</sub> may effect the reaction because of entropy factors; nevertheless one skilled in the art will appreciate the limits in size of any ring being formed. It is with the scope of the present reaction for a chelating ion to be used  
 5 to aid cyclization.

A further aspect of the present invention subsists in those complexes, which have simple axial ligands (water or halide) and a simple counter-ion (such as lithium). It is believed  
 10 that these ligands are environmentally and toxicologically more acceptable than ligands such as trifluoroacetate, tetra-phenylphosphonium and tetra-ethylammonium.

Accordingly, a further aspect of the present invention  
 15 provides a bleach activator having the structure:



wherein:

- 20
- B<sub>1</sub>, B<sub>3</sub> and B<sub>4</sub> each represent a bridging group having zero, one two or three carbon containing nodes for substitution, and B<sub>2</sub> represents a bridging group having at

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least one carbon containing node for substitution, each said node containing a  $C(R)$ ,  $C(R_1)(R_2)$  or  $C(R)_2$ ,

5 - each R substituent is the same or different from the remaining R substituents, and

10 (i) is selected from the group consisting of alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, alkynyl, alkylaryl, halogen, alkoxy, phenoxy and combinations thereof, or

(ii) form a substituted or unsubstituted benzene ring of which two carbons on the ring form nodes in the B-unit;

15 - M is a transition metal ion;

- L is an axial ligand selected from the group consisting of water and halide; and,

20 - Q is an alkali metal counter-ion.

It is also within the scope of the present invention to have a bleach activator, wherein M is selected from the group consisting of Fe, Mn, Cr, Cu, Co, Ni, Mo, V, Zn and W.

25

The present invention also extends to a packaged composition comprising a bleach activator as defined together with instructions for its use in a method of laundering fabrics.

30



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Detailed Description of the Invention

Throughout the description and claims generic groups are used, for example alkyl, alkoxy, aryl etc. Unless otherwise specified the following are preferred group restrictions that may be applied to generic groups found within compounds disclosed herein. Alkyl: linear and branched C1-C8-alkyl; alkenyl: C2-C8-alkenyl, cycloalkyl: C3-C8-cycloalkyl; cycloalkenyl: C4-12-cycloalkenyl having a single cyclic ring or multiple condensed rings and at least one point of internal unsaturation which can be optionally substituted with from 1 to 3 C1-C8-alkyl groups; aryl: selected from homoaromatic compounds having a molecular weight under 300, alkynyl: C2-C12-alkynyl; alkylaryl: C1-12-alkylaryl, wherein the aryl selected from homoaromatic compounds having a molecular weight under 300; halogen: selected from the group consisting of: F; Cl; Br and I; and, alkoxy: C1-C6-alkoxy.

Unless otherwise specified the following are more preferred group restrictions that may be applied to groups found within compounds disclosed herein. Alkyl: linear and branched C1-C6-alkyl; alkenyl: C3-C6-alkenyl; cycloalkyl: C6-C8-cycloalkyl; cycloalkenyl: C4-8-cycloalkenyl having a single cyclic ring or multiple condensed rings and at least one point of internal unsaturation which can be optionally substituted with from 1 to 3 C1-C8-alkyl groups; aryl: selected from group consisting of: phenyl; biphenyl; naphthalenyl; anthracenyl; and phenanthrenyl; alkynyl: C2-C8-alkynyl, alkylaryl: C1-6-alkylaryl, wherein the aryl is selected from selected from group consisting of: phenyl; biphenyl; naphthalenyl; anthracenyl; and phenanthrenyl; halogen: selected from the group consisting of: F and Cl; and, alkoxy: C1-C4-alkoxy.

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Preferred compounds of the present invention have R = methyl. B3 and B4 are preferably absent, the two related sides of the ring being derived from a 'classical' amino acid in which the amino group is located on the alpha-carbon. A preferred starting amino acid is 2-amino isobutyric acid. ( $\text{H}_2\text{N}-\text{C}(\text{CH}_3)_2-\text{COOH}$ ).

In the initial stage of the synthesis, the amino group of the acid is protected. The choice of protecting groups during synthesis to prevent undesirable reactions will be evident to one skilled in the art. For a discussion of protecting groups in organic synthesis the reader is directed to T. W. Green and P. G. M. Wuts, Protective Groups In Organic Synthesis 2nd Ed.; J. Wiley and Sons, 1991. Phthalic anhydride has been found to be a suitable protecting agent.

Activation of the carbonyl group following protection can be achieved by several means. One suitable means is reaction with a thionyl halide to yield the acyl halide. Reaction with an excess of thionyl chloride is preferred.

Following activation of the carbonyl, the protected macro-linker is formed by reaction with a diamine. The preferred diamines are phenylenediamines, preferably the o-phenylenediamine. These may be optionally substituted as described in the patents of Collins et al., as mentioned above. It is preferred to use the unsubstituted diamine.

The protected amino groups of the macro-linker may be unprotected by any suitable reaction. Where phthalic anhydride has been used as the protecting agent the de-

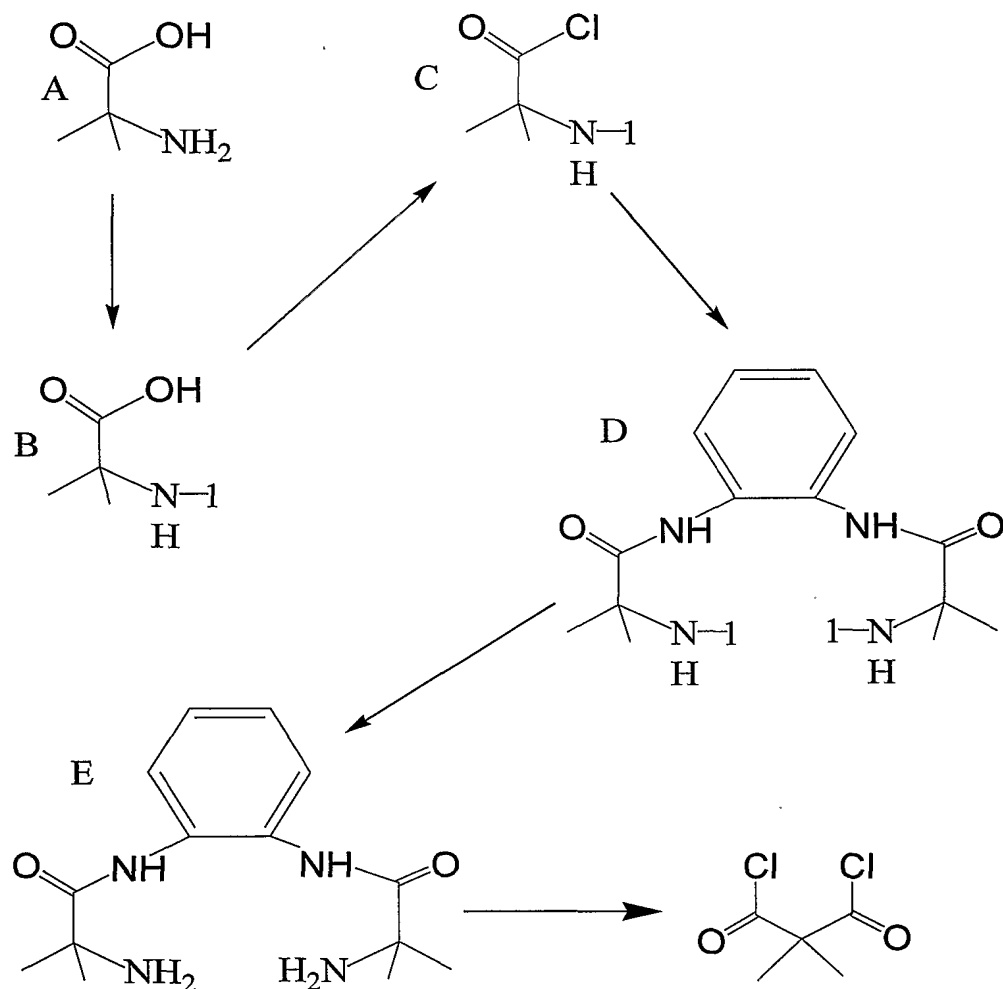
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protection can conveniently be accomplished through treatment with hydrazine hydrate.

Ring closure is conveniently obtained through reaction of the macro-linker with a di-carbonyl species, which has been activated. Preferably, B1 comprises a single substituted carbon atom. It is preferred that the portion of the heterocycle ring comprising B1 is derived from a malonate or oxalate. B1 most preferably is  $-(\text{Me})_2\text{C}-$ . Dimethylmalonyl chloride is a suitable reagent. It is preferable that the ring closure reaction is performed slowly and at high dilution to prevent the formation of side products.

The following schematic shows a reaction scheme for the synthesis of a compound according to a preferred embodiment of the present invention. The individual reactions are described in more detail below. The amino acid, 2-aminoisobutyric acid, 'A', is reacted with a protecting agent to form a derivative with a protected amino group 'B'. The carbonyl group of the protected amino acid is then activated to form species 'C'. Reaction of two moles of 'C' with a mole of o-phenylene diamine yields the derivative 'D', which is subsequently deprotected at '1' to give the macro-linker 'E'. One skilled in the art will understand that differing protective groups may be used in the reaction, nevertheless a use of a single type of protecting group is preferred. Species 'E' is reacted with dimethyl malonyl chloride to close the ring structure and produce the final ligand (not shown). Metallisation of the ligand gives the active catalyst.

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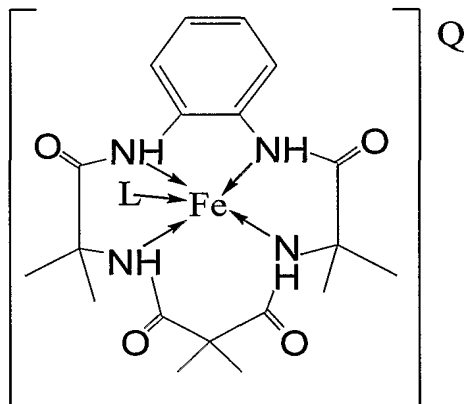


Metallation of the ligand is preferably performed under  
 5 nitrogen and in a non-aqueous solution such as dry  
 tetrahydrofuran (THF). The transition metal is preferably  
 selected from groups VI, VII, VIII, IX, X and XI of the  
 periodic table. More preferably the metal is selected from  
 the group consisting of Fe, Mn, Cr, Cu, Co, Ni, Mo, V, Zn  
 10 and W. Particularly preferably the metal is selected from  
 the group comprising: Fe, Mn, Cu and Co. Iron is the most  
 preferred metal.

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Suitable counter ions are K, Li or Na, most preferably lithium.

The most preferred compound is that in which the ligand is  
 5 5,6-benzo-3,8,11,13-tetraoxo-2,2,9,9,12,12-hexamethyl-  
 1,4,7,10-tetraazacyclotridecane as shown below as the Fe  
 form, the axial ligand 'L' is water or preferably chloride.  
 The counter-ion 'Q' is preferably lithium. This can also be  
 described as 3,4,8,9-tetrahydro-3,3,6,6,9,9-hexamethyl-1H-  
 10 1,4,8,11-benzotetraazocyclotridecane-2,5,7,10 (6H,11H)  
 tetrone.



The present invention also extends to fully formulated  
 15 products containing the catalysts disclosed herein. Such  
 products will generally contain a detergent active and will  
 typically contain one or more builders together with the  
 typical additive used in detergent compositions.

20 Typical levels of the catalyst of the present invention in  
 fully formulated compositions will range from 0.00005 to 2  
 wt.% with 0.005 to 1 wt.% being particularly preferred and  
 0.05 to 0.5 wt.% being most particularly preferred. Typical

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levels of peroxygen source in fully formulated composition will range from 0.05 to 55 wt.% with 1 to 40 wt.% being particularly preferred and 5 to 25 wt.% being most particularly preferred. Preferred peroxygen sources include percarbonate and perborate.

### Examples

10 In order that the invention may be further and better understood it will be described in detail with reference to following non-limiting examples.

#### 15 **Example 1: Preparation of 2-Methyl 2-phthalimidopropanoic acid**

Phthalic anhydride (1 Kg, 4.84 mol) and 2-aminoisobutyric acid (500 g, 6.75 mol) were pre-mixed and heated to 190 °C with stirring. Once molten, the reaction was held at this temperature until no further water was expelled, approximately 4 hours. The reaction mixture was poured into large crystallising dishes and, whilst still hot, neutralised with 10 % aqueous sodium bicarbonate solution (12.5 L). The mixture was then filtered to remove any insolubles. The filtrate was acidified with concentrated hydrochloric acid until a thick white precipitate was observed. The precipitate was filtered and washed with water to remove remaining hydrochloric acid from the precipitate. The precipitate was dried under vacuum to yield the title compound as a white powder (974 g, 86%).

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<sup>1</sup>H NMR (500 MHz, d<sup>6</sup> acetone) 7.84 (m, 4H), 1.83 (s, 6H); <sup>13</sup>C NMR (125 MHz) 24.87, 60.87, 123.64, 132.73, 135.19, 168.92, 174.26.

5    **Example 2: Preparation of 2-Methyl-2-phthalimidopropanoyl chloride**

Thionyl chloride (750 ml, 10.28 mol) was added to 2-methyl-2-phthalimidopropanoic acid (385 g, 1.65 mol) and the  
10 mixture refluxed under nitrogen for 3 hours. Excess thionyl chloride was removed under reduced pressure to yield a solid. The solid was washed with diethyl ether (2 x 250 ml) to yield the title compound as a white crystalline solid (408.2 g, 98%).

15

<sup>1</sup>H NMR (500 MHz, d<sup>6</sup> acetone) 7.92 (m, 4H), 1.95 (s, 6H); <sup>13</sup>C NMR (125 MHz) 24.32, 68.41, 124.20, 132.45, 135.78, 168.48, 175.37.

20    **Example 3: Preparation of N,N'-1,2-phenylenebis[2-methyl-2-phthalimidopropanamide]**

A solution of *o*-phenylene diamine (34.4 g, 0.32 mol) and triethylamine (75 ml) in THF (1 L) was added drop-wise to a  
25 stirred solution of 2-methyl-2-phthalimidopropanoyl chloride (160 g, 0.63 mol) in THF (1.5 L) at a temperature of 0 °C. After addition the reaction was warmed to room temperature and stirred for a further 12 hours and then refluxed for a further 2 hours. The reaction mixture was cooled in ice,  
30 filtered and the THF removed under reduced pressure. The resultant white solid was dissolved in dichloromethane (1.5 L) and washed with 1 M hydrochloric acid (3 x 1 L) followed by washing with a 5 % sodium bicarbonate solution. The

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dichloromethane extract was dried ( $\text{MgSO}_4$ ), filtered and stripped of solvent under reduced pressure to yield the title compound (149.72 g, 87%).

5  $^1\text{H}$  nmr (500 MHz,  $\text{d}^6$  DMSO) 9.41 (s, 2H), 7.83 (d,d, 4H,  $^3\text{J} = 5.45$  Hz,  $^4\text{J} = 3.04$  Hz), 7.76 (d,d, 4H,  $^3\text{J} = 5.45$  Hz,  $^4\text{J} = 3.04$  Hz), 7.51 (m, 2H), 7.17 (m, 2H), 1.73 (s, 12H);  $^{13}\text{C}$  nmr (125 MHz) 24.70, 61.44, 123.21, 124.60, 125.46, 130.85, 132.00, 134.82, 168.66, 171.99.

10

**Example 4: Preparation of N,N'-1,2-phenylenebis[2-methyl-2-methylpropanamide]**

A stirred suspension of the protected diamide diamine (N,N'-1,2-phenylenebis [2-methyl-2-phthalimidopropanamide] (141 g, 0.26 mol) in ethanol (3 L) was refluxed and treated with hydrazine (33.7 mL, 0.69 mol). The suspension dissolved after a few minutes and the reaction mixture refluxed for a 15 hours during which a white precipitate was formed. The reaction was cooled to room temperature and the ethanol was removed under reduced pressure to yield a solid. The solid was dissolved in 2 M hydrochloric acid (8.812 L) and heated at 80 °C for an hour and then cooled to room temperature. The reaction mixture was then filtered and the filtered 20 liquid adjusted to pH 13 with a concentrated sodium hydroxide solution to yield a deep yellow colour solution. The deep yellow colour solution was extracted with 25 dichloromethane (3 x 2 L), and the combined extracts dried ( $\text{MgSO}_4$ ). Removal of solvent under reduced pressure gave an off white solid which was washed with ether (1 L) to yield 30 the title compound as a white solid (69.2 g, 95%).



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<sup>1</sup>H nmr (500 MHz, d<sup>6</sup> DMSO) 7.66 (m, 2H), 7.2 (m, 2H), 4.75 (brs), 1.36 (s, 12H); <sup>13</sup>C nmr (125 MHz) 29.03, 55.27, 124.41, 125.15, 131.32, 177.09.

5 **Example 5: Preparation of 3,4,8,9-tetrahydro -3,3,6,6,9,9-hexamethyl-1H-1,4,8,11-benzotetraazocyclotridecane-2, 5,7,10 (6H,11H) tetrone.**

10 The following reaction was conducted under nitrogen with vigorous stirring of the reaction mixture. Individual solutions of dimethylmalonyl chloride (18.2 g) in 1L THF and a mixture of N,N'-1,2-phenylenebis[2-methyl-2-methylpropanamide] (30g, 0.11 mol) and triethylamine (31mL)  
15 in THF (1L) were added in a controlled manner over 10 hours to THF (750 mL) whilst maintaining the reaction mixture at 0°C. During the reaction a precipitate was formed and the reaction mixture warmed to room temperature overnight. The reaction mixture was filtered, the precipitate washed with  
20 water (4 x 500 mL) and dried under reduced pressure to yield the title compound (40.3 g, 100%).

<sup>1</sup>H nmr (500 MHz, d<sup>6</sup> DMSO) 8.35 (brs, 2H), 7.74 (brs, 2H), 7.47 (m, 2H), 7.16 (m, 2H), 1.47 (s, 12H), 1.45 (s, 6H); <sup>13</sup>C  
25 nmr (125 MHz) 22.70, 25.48, 51.05, 125.12, 125.58, 130.54, 172.45, 173.23.

**Example 6: Metallation of 3,4,8,9-tetrahydro-3,3,6,6,9,9-hexamethyl-1H-1,4,8,11-benzotetraazocyclotridecane-2, 5,7,10 (6H,11H) tetrone.**  
30

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A stirred suspension of 3,4,8,9-tetrahydro-3,3,6,6,9,9-hexamethyl-1H-1,4,8,11-benzotetraazocyclotridecane-2,5,7,10 (6H,11H) tetrone (5 g) in THF (1 L) under a nitrogen atmosphere was heated to 40 °C. The heated suspension was then treated with 31 mL butyl lithium causing the suspension to dissolve; 30 minutes after the treatment iron (II) chloride was added. After 36 hours the reaction mixture was cooled and filtered to provide a solid. The solid was dissolved in water (1 L) yielding a solution of pH 12 which was stirred and treated with a lithium hydroxide solution (1.5 mL) followed by addition of concentrated hydrochloric acid until the pH of the solution was 5 (colour change from brown to red/orange). The pH of the solution was then adjusted to pH 7 by addition of a lithium hydroxide solution and the solvent removed under reduced pressure to yield a sticky orange solid. The sticky orange solid was washed with methanol to provide a powder. The powder was purified by dissolution in ethanol and elution through a Florisil™ column with acetonitrile to yield the title compound.

#### Wash Examples

In the Following wash Examples 7 to 9 a 'base' colour washing powder with approximately the following composition was used (all percentages by weight). This 'base' differs slightly from commercial powders in that it does not contain colour care components. Otherwise, the composition is very similar to that of products available at present in the marketplace.

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	Sodium linear alkyl (C12) benzene sulphonate	7.9%
	C12-14 Nonionic 7EO	5.1%
	C12-14 Nonionic 3EO	4.0%
	Soap	0.35%
5	Fatty Acid	0.40%
	Sodium tripolyphosphate	30.0%
	Sodium silicate	7.9%
	Sodium sulphate	14.5%
	Sodium hydrogen carbonate	4.0%
10	Sodium carbonate	8.8%
	Minors and water	to 100%

Minors included an antifoam agent, a soil release polymer, protease, lipolase, amylase and perfume.

15

Colour of test samples are expressed in terms of  $\Delta E$ . For further detail of this measurement the reader is directed to "Measuring Colour" by R.W.G. Hunt, Series in Applied Science and Industrial Technology, Ellis Horwood, (1976) and in particular page 76 in which the CIELAB colour difference equation is given.

20

The following experiments were performed in what is known as "over the side experiments"; the components as detailed were added separately via the draw of the washing machine to the wash.

25

#### **Example 7: Washing Experiment**

The Base colour washing powder (105g) was placed in the drawer of a Miele Novotronic (RTM) European-type horizontal-axis washing machine and the machine used to wash a 2.566 kg

30

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wash load. The load comprised 1250g non-mercerised white cotton sheeting, 1250g 50:50 white polycotton sheeting, and 5 x 900cm<sup>2</sup> green cloth, 'direct green 26' at 5%, unfixed, weighing 66g. The wash was conducted using the machines 40°C program and 26° French hard water.

After the wash the cloths were tumble dried and examined. Visual examination revealed that both the white cotton and poly-cotton sheeting had both become green due to pick up of dye lost from the direct green cloth. Measurement of the CIELAB  $\Delta E$  value of the cotton cloth compared to the original white gave a value of 10.5.

The experiment was repeated with fresh cloth but in the presence of 0.035g of the catalyst prepared in example 6 and 3.63g of a 35% solution of H<sub>2</sub>O<sub>2</sub> was added. The CIELAB  $\Delta E$  value of the cotton cloth compared to the original white was 2.4. Visual examination showed that the amount of green dye transferred to the white cloths had been significantly reduced.

#### **Example 8: Washing Experiment**

The protocol of example 7 was followed except the wash load consisted of 2.566kg of a soiled load (dirty tea towels, pillow cases and towels, all 100% white cotton; 10 400cm<sup>2</sup> clean white cotton monitor cloths; 5 900cm<sup>2</sup> green cloth, dyed with direct green 26 at 5%, unfixed.

After the washing and drying the white cotton cloths showed transference of the green dye on visual inspection. The

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CIELAB  $\Delta E$  value of the cotton monitor cloth compared to the original white was 7.4

The experiment was repeated with fresh cloth but with the levels of catalyst prepared in example 6 and levels of an aqueous 35% solution of  $H_2O_2$  added as shown in Table 1 below. The average CIELAB  $\Delta E$  value of the cotton monitor cloths at the various levels of catalyst and peroxide are given in Table 1 below. It can be seen that catalyst has reduced dye transfer when present.

Table 1

Added catalyst in grams	Added $H_2O_2$ (35%) in grams	Measured $\Delta E$
0	0	7.4
0.035	3.63	4.0
0.035	14.57	4.4
0.070	14.52	3.7

**Example 9: Washing Experiment**

The protocol of example 7 was repeated, except the load consisted of 1.5kg of white Terry towelling, 600g cotton sheeting, 400g of 1% unfixed Direct Black 22 cotton cloth.

When washed without the catalyst being present the white cloth became visibly grey, and the CIELAB  $\Delta E$  value of the cotton sheeting was 14.4 compared to the original. When the

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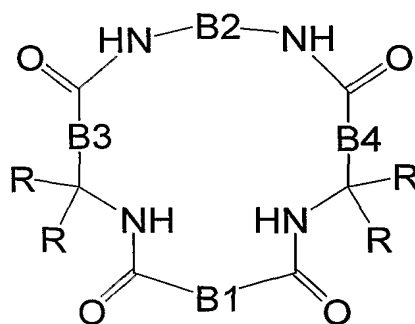
catalyst was added at levels of 0.0035g with 0.36g of a 35% solution of  $H_2O_2$ , the CIELAB  $\Delta E$  value of the cotton sheeting was 6.5 compared to the original. It can again be seen that dye transfer had been considerably reduced in the presence  
5 of the catalyst.

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CLAIMS

1. A method for the synthesis of a ligand having the structure:

5



wherein:

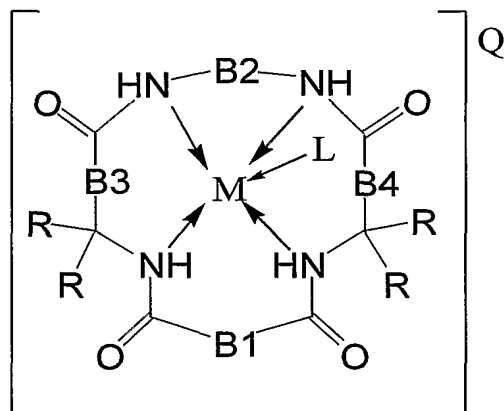
- 10        -     $B_1$ ,  $B_3$  and  $B_4$  each represent a bridging group having zero, one two or three carbon containing nodes for substitution, and  $B_2$  represents a bridging group having at least one carbon containing node for substitution, each said node containing a  $C(R)$ ,  
 15         $C(R_1)(R_2)$  or  $C(R)_2$  ,
- each R substituent is the same is the same or different from the remaining R substituents and
- 20        (i) is selected from the group consisting of alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, alkynyl, alkylaryl, halogen, alkoxy, phenoxy and combinations thereof, or

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(ii) form a substituted or unsubstituted benzene ring  
of which two carbons on the ring form nodes in  
the B-unit,  
said method comprising the steps listed below in the  
order given

- a) protecting the amino group of an amino acid  
comprising  $\text{HOOC-B}_3\text{-CRR-NH}_2$  and/or  $\text{HOOC-B}_4\text{-CRR-NH}_2$ ,
- b) activating the carbonyl group of said amino acid,
- c) reacting the carbonyl-activated amino acid with a  
diamine  $\text{H}_2\text{N-B}_2\text{-NH}_2$  to form a diamide diamine,
- d) deprotecting said protected amino groups, and,
- e) reacting the de-protected diamide diamine with an  
activated di-carbonyl compound to form a tetra-amine  
macrocycle.

2. A bleach activator having the structure:





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wherein:

-  $B_1$ ,  $B_3$  and  $B_4$  each represent a bridging group having zero, one two or three carbon containing nodes for substitution, and  $B_2$  represents a bridging group having at least one carbon containing node for substitution, each said node containing a  $C(R)$ ,  $C(R_1)(R_2)$  or  $C(R)_2$ ,

- each R substituent is the same is the same or different from the remaining R substituents and

(i) is selected from the group consisting of alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, alkynyl, alkylaryl, halogen, alkoxy, phenoxy and combinations thereof, or

(ii) form a substituted or unsubstituted benzene ring of which two carbons on the ring form nodes in the B-unit,

- M is iron, cobalt or manganese

- L is an axial ligand selected from the group consisting of water and halide

- Q is an alkali metal counter-ion

3. A method according to claim 1, wherein R = methyl.

4. A method according to claim 1, wherein  $B_3$  and  $B_4$  are absent.

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5. A method according to claim 1, wherein  $B3 = B4$ .
6. A composition comprising a bleach activator according to  
5 claim 2, wherein the M is Fe.
7. A composition comprising a bleach activator according to  
claim 5, wherein Q is Li.
- 10 8. A composition comprising a bleach activator according to  
claim 2, together with a detergent and a peroxy source.
9. A method of inhibiting dye transfer in a wash comprising  
the steps of washing a fabric in the presence of a  
15 bleach activator according to claim 2 and a peroxy  
source.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 01/09351

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D257/10 C11D3/39

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D C11D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 099 586 A (HORWITZ COLIN P ET AL) 8 August 2000 (2000-08-08) * col. 2, l. 15-18, l. 59-63; col. 7, l. 34-53; example 19; claim 1 -----	2,6-9



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

\* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&amp;\* document member of the same patent family

Date of the actual completion of the international search

23 November 2001

Date of mailing of the international search report

03/12/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

JOHNSON, C

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-9 (part)

Present claims 1-9 relate to an extremely large number of possible compounds, compositions and methods, and the exact scope of these claims is not clear. This lack of clarity arises because of the definitions of B1-B4. It is not clear whether "a carbon containing node" can contain other atoms, and in the definition "a carbon containing node for substitution" it is not clear whether this substitution is a reference to the R groups or to further possible substitution. Furthermore, there is no upper limit for the size of the B2 group. The description does not provide a clear explanation of how to interpret the definitions of B1-B4; indeed it is stated on p. 5 that the B groups are not limited to those defined in the claims. The lack of clarity within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear, namely compounds, compositions and methods wherein B1, B3 and B4 represent bridging groups with 0-3 C(R), C(R1)(R2) or C(R)2 groups in which the R substituents are defined as in claim 1 and wherein B2 represents a bridging group with 1-2 C(R), C(R1)(R2) or C(R)2 groups (the upper limit of B2 having been taken from the example in the description).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

In tional Application No

PCT/EP 01/09351

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